62. (New) The carrier according to claim 61 pre-treated to contain components found in an animal fluid.

63. (New) The carrier according to claim 62 wherein the pre-treatment is by immersion in a solution containing components found in an animal fluid for a period of up to about seven days prior to use.

64. (New) The carrier according to claim 63 wherein the animal fluid is interstitial fluid.

65. (New) The carrier according to claim 64 wherein the carrier is synthesized under sterile conditions or sterilized subsequent to synthesis using conventional sterilization methods.

REMARKS

The Official Action dated January 30, 2002, has been carefully considered. It is believed that the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

Claims 1-13 have been canceled, without prejudice or disclaimer thereof, and claims 50-65 have been added to the application. Because the new claims do not introduce new matter, entry thereof by the Examiner is respectfully requested.

It is acknowledged that claims 1 – 13 are currently under consideration by the Examiner and that the remaining groups of claims may be rejoined upon allowance of the elected claims.

I. Rejections of the Claims Under 35 USC § 112

The Examiner rejected claims 1-13 as being indefinite for failing to particularly point out and distinctly claim the subject matter Applicants regard as the invention. Applicants traverse this ground for rejection.

The Examiner rejected claim 2 as being a duplicate of claim 1. Applicants have cancelled claim 2.

In addition, the Examiner rejected claim 5 on the basis that "the material" lacks antecedent support. Applicants have cancelled claim 5.

Applicants submit that the claims as currently amended overcome this rejection.

II. Rejections of the Claims Under 35 USC § 102

The Examiner rejected claims 1-13 as being anticipated by each of: Duscheyne et al. (WO 96/03117A1); Latorre et al. (WO 99/07777); Sankaram (US 6,277,413B1); Staas et al. (US 6,312,731); Guillen (US 6,074,673); O'Hagan (US 5,603,960); Bernstein et al. (US 5,679,377); and Jou et al. (US 5,866,322). Applicants traverse this ground for rejection.

The claims have been amended without prejudice. It is submitted that the claims as amended overcome the prior art cited by the Examiner.

The present invention describes a carrier comprising a biomolecular interaction. The carrier has many uses including use in an assay for screening of modulators of the said biomolecular interaction. A biomolecular interaction is defined at page 10 of the application as comprising any two or more biological species. These species can interact, and each species can potentially further comprise additional subunits or interacting moieties. An example of such biomolecular interactions are protein-protein interactions, such as a monomeric protein with another monomeric protein and a multimeric protein with another mono or multimeric protein. In one embodiment, the interaction can be an enzyme/effector interaction, a receptor/promoter interaction, or the like. First, the biomolecular interaction is entrapped in a carrier (or matrix). The carrier and conditions for entrapping the biomolecular interaction are selected to preferably obtain one or more of the following features (see for example page 20 of the description):

(i) to permit the biomolecular interaction and subunits thereof to retain their bioactivity, so that conformational changes in the biomolecular interaction and units thereof can occur, in accordance with changes in physical or chemical parameters of the system;

(ii) to enable the passage of small molecules/peptides through the matrix but inhibit the leakage of the components of the bimolecular interaction; and

(iii) to permit the denaturation and renaturation of the biomolecular interaction under controlled conditions, such that aggregation of the components does not occur until or unless desired (the reversibility of the assay).

The entrapped intact interaction can subsequently be used to screen for modulators of the interaction, and as such is a target for drug screening. In a preferred embodiment, this is accomplished, for example, by encapsulating the biomolecular interaction in a carrier; denaturing the biomolecular interaction while inhibiting the irreversible aggregation of the components of the biomolecular interaction; administering the potential modulator; adjusting the conditions to permit for renaturation of the biomolecular interaction; and detecting renaturation or the lack thereof of the biomolecular interaction depending on the action of the modulator.

This is different and patentably distinct from the references cited by the Examiner. None of the references cited by the Examiner describe a carrier comprising a biomolecular interaction entrapped within the matrix, wherein the biomolecular interaction comprises two or more biological species that can be reversibly dissociated from the other.

WO 96/03117 ('117) to Ducheyne describes the incorporation of a bioactive molecule such as vancomycin or a growth factor into a silica-based carrier using a sol-gel process for controlled release of the bioactive molecule. To affect the controlled release, the matrix has granules in the range of 500 micrometers to about 5 millimeters (p. 13, lines 9-10). The molecules are designed to be released over time when immersed in solutions containing, for example, ions typical of interstitial fluid (p. 15, line 37). Bioactive is defined in the application as a bone bioactive material having a calcium phosphate rich layer (p. 16, lines 9-10). The invention is preferably used in the restoration of bone. There is no teaching in Ducheyne of the reversible denaturation in a carrier of a biomolecular interaction as defined in the present invention, or of a carrier comprising such features. Further there is no teaching in Ducheyne of use of a carrier comprising a protein or other molecule in a screening assay.

The present invention is not used for the controlled release of a molecule *in vivo*. The matrix of the present invention comprises a biomolecular interaction that comprises two or more biological species that can reversibly dissociate (or for that matter reversibly associate) within the matrix itself. As such the carrier preferably inhibits leaching out (or

release) of the biomolecular interaction or components thereof. Further, in the present invention, screening of the potential modulators occurs within the carrier comprising the interaction, as such the release of such molecules is not desired. This assists in the reproducibility of measurements of the fluorescent signals.

Last, the claims of the '117 patent application specify TMOS only, vancomycin, growth factor TGF-b, or anti-inflammatory or analgesic only, and controlled release only as parts of the new invention.

WO 99/07777('777) to Latorre describes compositions comprising a glass composition and a biodegradable polymer and methods of preparation and use thereof for growing tissue, including bone. The '777 patent application builds on the '117 patent application and extends the claims to other growth factors. There is no mention of entrapping a biomolecular interaction, reversibly denaturing the biomolecular interaction or screening for modulators of the biomolecular interaction as in the present invention. Further, biodegradable polymers in the '777 patent application, are different from the present materials. The entrapped proteins again are single proteins (perhaps made up of individual non-active subunits), but are not biomolecular interactions as defined in the present application.

US 6,277,413B1 to Sankaram describes a biodegradable polymer for controlled release of components. As stated above, in the carrier of the present invention the biomolecular interaction is entrapped within the matrix of the carrier and is not designed for controlled release.

US 6,312,731 to Staas describes a material that has the potential to either dissolve or swell rapidly to allow release of entrapped components so that an immune response is obtained. The carrier of the present invention is not designed to allow release of entrapped components. If implanted, the carrier of the present invention would not illicit an immune response since the bioactive components would remain entrapped.

US 6,074,673 to Guillen also teaches a controlled release delivery system, which again is distinct from the carrier of the present invention that is designed to retain entrapped components.

US 5,603,960 to O'Hagan describes polymer microspheres that have an internal aqueous compartment that contains a pharmaceutical composition which must be released

from the microsphere to have any pharmacological effect. The carrier of the present invention comprises a biomolecular interaction that is entrapped within the carrier matrix.

US 5,679,377 to Bernstein describes a biodegradable polymer prepared by cross-linking of proteins into microspheres which is used for controlled release *in vivo*. As described above, this is distinct from the carrier of the present invention that involves retention of entrapped components.

US 5,866,322 to Jou describes a capture polymer that retains an antibody via cationic capture for detection of rubella. The matrix described by Jou has a large pore network to allow flow of large molecules such as antibodies into the matrix, and to produce liquid-phase kinetics. The carriers of the present invention do not permit the entry of large biomolecules owing to the entrapment of the biomolecular interaction and thus an inherently smaller pore size.

To summarize, none of the prior art cited by the Examiner describes a carrier having a biomolecular interaction as defined in the present invention, wherein the biological species of the biomolecular interaction are entrapped within the carrier and can be reversibly dissociated within the carrier. Nor does any of the prior art describe a carrier comprising a biomolecular interaction that can be used in screening assays.

III. Conclusion

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

If there are any fees due in connection with the filing of this Amendment, please charge the fees to our Deposit Account No. 19-0741. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date July 29, 2002

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